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Experimental Inoculation of Growing Pigs with U.S. Strains of Swine and Human Hepatitis E Viruses

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Abstract
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Experimental Inoculation of Growing Pigs with U.S. Strains of Swine and Human Hepatitis E Viruses

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Summary and Implications

U.S. strains of swine and human hepatitis E viruses (HEV) are closely related genetically. We found that swine and human HEV differ in virulence and both induce subclinical, but morphologically discernable, hepatitis in experimentally infected SPF pigs. Experimental inoculation of pigs with human HEV may provide a useful model to study the pathogenesis of hepatitis E virus infection and test efficacy of human HEV vaccines.

Introduction

Swine hepatitis E virus (HEV) was discovered in 1997 (1). Further analysis of the virus revealed that swine HEV is antigenically and genetically closely related to recent U.S. strains of human HEV (2). Genetic and experimental evidence for cross-species infection by swine hepatitis E virus has been recently reported (2). Pigs are considered a potential reservoir of HEV. Veterinarians, pork producers, pig handlers, and pork processors may be at risk of zoonotic infection by swine HEV. There is also concern over inadvertent transmission of swine HEV in pig organs or tissues that are transplanted to humans (xenotransplantation). This research project was initiated to develop a model to better understand the pathogenesis of infection of pigs with swine and human HEV.

Materials and Methods

Three-week-old, specific pathogen free (SPF) pigs were inoculated with hepatitis E virus (HEV) to evaluate the pathogenicity and sites of virus replication. Group 1 (n=17) remained as uninoculated controls, group 2 (n=18) was intravenously inoculated with HEV recovered from a pig, and group 3 (n=19) was inoculated with HEV recovered from a human (US-2 strain, kindly provided by Isa Mushahwar, Abbott Laboratories, IL). Two to four pigs per group were necropsied at 3, 7, 14, 20, 27, and 55 days post-inoculation (DPI). Three pigs per group were monitored weekly by serum chemistry profiles (AST, ALT, GGT, SDH and total bilirubin) for evidence of liver damage.

Results and Discussion

There was no evidence of clinical disease or remarkable elevation of liver enzymes or bilirubin in any of the groups. Seroconversion to HEV occurred in 0/7, 5/8, and 9/9 pigs by 27 DPI in groups 1 – 3, respectively. By 42 DPI, 0/4, 4/5, and 6/6 of the remaining pigs were seropositive for anti-HEV antibodies. The presence of HEV genome in feces, sera, bile, and liver is being tested by reverse transcription-polymerase chain reaction (RT-PCR). Hepatitis lesions were very mild and multifocal in group 1 pigs, mild-to-moderate in group 2 pigs, and moderate-to-severe in group 3 pigs. Multifocal lymphoplasmacytic hepatitis was observed in 9/17, 15/18, and 16/19 of the pigs in groups 1 – 3, respectively. Focal hepatocellular necrosis was observed in 5/17, 10/18, and 13/19 of the pigs in groups 1 – 3, respectively. Hepatic inflammation and hepatocellular necrosis peaked in severity at 20 DPI and was still moderately severe at 55 DPI in the group inoculated with human HEV (group 3).

Swine and human HEV differ in virulence and both induce subclinical, but morphologically discernable, hepatitis in experimentally infected SPF pigs. The model described in this report may provide a useful animal model to study HEV infection. Swine HEV also may prove to be useful in developing vaccines against HEV infections of humans.

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References

1. X.-J Meng., R. H. Purcell, P. G. Halbur, J. R. Lehman, D. M. Webb, T. S. Tsareva, J. S. Haynes, B. J. Thacker, S. U. Emerson. 1997. A novel virus in swine closely related to the human hepatitis E virus. Proc. Natl. Acad. Sci. USA 94: 9860 – 9865.
2. Meng X.-J., P. G. Halbur, M. S. Shapiro, S Govindarajan, J. D. Bruna, I. K Mushahwar, R. H. Purcell, S. U Emerson. 1998. Genetic and experimental evidence for cross-species infection by swine hepatitis Evirus. J. Virol. 72(12):9714-9721.